Interview Summary

09/451,641	GAO ET AL.
Examiner	**Art Unit**
Susan Tran	1615

All participants (applicant, applicant's representative, PTO personnel):

(1) *Susan Tran*.

(2) *James C. Forbes*.

(3) *Kenton Fedde*.

(4) ~~*Padmanabhan Sreenivasan*~~

Date of Interview: *23 October 2003* .

Type: a)☐ Telephonic b)☐ Video Conference
c)☒ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: ____ .

Claim(s) discussed: *of record* .

Identification of prior art discussed: *of record* .

Agreement with respect to the claims f)☐ was reached. g)☒ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *See Continuation Sheet* .

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

i)☒ It is not necessary for applicant to provide a separate record of the substance of the interview(if box is checked).

Unless the paragraph above has been checked, THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

_____
Examiner's signature, if required

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR § 1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case unless both applicant and examiner agree that the examiner will record same. Where the examiner agrees to record the substance of the interview, or when it is adequately recorded on the Form or in an attachment to the Form, the examiner should check the appropriate box at the bottom of the Form which informs the applicant that the submission of a separate record of the substance of the interview as a supplement to the Form is not required.

It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments:

Applicant pointed out that [illegible] [illegible] [illegible] [illegible] [illegible] the claimed invention [illegible] [illegible] [illegible] that the relative bioavailability is obtained by the use of micron size particulate [illegible].

Applicant will amend the claims to incorporate the particle size limitation of claim 5 into the [illegible] claim. Proposed claim is allowable over the [illegible] prior art. Applicant will file an immediate response and submit prior art (IDS).

Thurman K. Page, M.A., J.D.
Supervisory Patent Examiner
Art Unit 1615
Technology Center 1600

Claim 1 (dissected)

A pharmaceutical composition comprising:

(1) one or more discrete solid orally deliverable dose units

each comprising

(2) particulate celecoxib

(3) in an amount of about 10 mg to about 1000 mg

(4) in intimate mixture with one or more pharmaceutically acceptable excipients,

(5) said composition exhibiting upon oral administration a relative bioavailability not less than about 50% by comparison with an orally delivered solution containing celecoxib at the same dosage rate.

Black (EP 0 863 134)

Discloses:

(1) discrete solid orally deliverable dose units (tablets, *etc.*)

each comprising

(2) a selective COX-2 inhibitory compound, not celecoxib

– no disclosure of particle size <200 μm taught by Applicant to give acceptable bioavailability

(3) in an amount of 10 mg to about 250 mg

(4) in intimate mixture (*e.g.*, prepared by wet granulation) with one or more pharmaceutically acceptable excipients

– no disclosure of specific excipients illustratively shown in Applicant's specification to be associated with high bioavailability (wetting agent, polyvinylpyrrolidone)

(5) relative bioavailability not disclosed

Black does not render the invention (as embodied in Claim 1) obvious under 35 USC 103(a)

1. A *prima facie* case has not been made (MPEP 2143)
   - no suggestion or motivation to modify the reference
     - Black fails to suggest desirability of the invention, namely high relative bioavailability *(In re Fine)*
   - no reasonable expectation of success
     - textbook teaching predicts low relative bioavailability of a highly insoluble drug in a discrete solid dosage form (Remington, p. 742)
   - all claim limitations not taught or suggested
     - no teaching or suggestion in Black of
       (a) celecoxib
       (b) relative bioavailability not less than 50%
       (c) any of the means shown illustratively in Applicant's specification to enhance bioavailability

ABSOLUTE BIOAVAILABILITY

Absolute bioavailability: ratio of AUC for specific oral composition to AUC of same dose given intravenously

- oxaprozin 95%
- naproxen 95%
- celecoxib 17% (unformulated – worst case)
  57–89% (oral solution – best case)

see specification, p. 47, Table 11-1; p. 50, Tables 11-2C,D

RELATIVE BIOAVAILABILITY

Relative bioavailability: ratio of AUC for specific oral composition to AUC of a reference dosage form (in this case oral solution)

- celecoxib unformulated 19–30%

see specification, p. 47, Table 11-1; p. 50, Tables 11-2C,D

- celecoxib suspension (1 micron) ~100%

see specification, p. 50, Tables 11-2C,D

- celecoxib 100 mg tablet (X2) ~95%
- celecoxib 200 mg tablet ~98%

see specification, p. 63, Table 18B

Black does not render the invention (as embodied in Claim 1) obvious under 35 USC 103(a)

2. Even if it had been obvious to try, what would the skilled artisan expect by substituting celecoxib for Black's compound?
   - celecoxib is highly insoluble
   - celecoxib has relatively low absolute BA (57–89% for oral solution)
   - unformulated celecoxib has very low relative BA
   - textbook teaching suggests:

> "A drug usually has the highest bioavailability if administered orally as an aqueous solution; finely comminuted drugs in suspension follow closely. However, as a drug is packed into hard gelatin capsules or compacted into tablets, its bioavailability decreases."
>
> (Remington, p. 742)

Black does not render the invention (as embodied in Claim 1) obvious under 35 USC 103(a)

expected result	observed result
low BA relative to oral solution	high (at least about 50%) BA relative to oral solution
- standard textbook teaching	- versus 19–30% when unformulated

Proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. *In re Hedges;* MPEP 2145.X.D.3

Black does not render the invention (as embodied in Claim 1) obvious under 35 USC 103(a)

3. Secondary indicia of nonobviousness:

Major commercial success of a capsule composition of the invention, marketed as CELEBREX by Pharmacia Corp. and Pfizer Inc.

- safe and effective therapy for arthritis and other COX-2 mediated inflammatory conditions would have been missed or seriously delayed had the present inventors not gone against accepted wisdom in attempting to formulate in a discrete solid dosage form such an insoluble drug exhibiting low absolute BA

(*Graham v. Deere; In re Piasecki;* MPEP 2144.08 II.B)

Possible amended Claim 1 (*cf.* granted European patent EP 1 049 467 B1)

1. (Twice amended) A pharmaceutical composition comprising one or more discrete solid orally deliverable dose units, each comprising particulate celecoxib in an amount of about 10 mg to about 1000 mg in intimate mixture with one or more pharmaceutically acceptable excipients, and having a distribution of celecoxib particle sizes such that D_{90} of the particles is less than 200 μm; said composition exhibiting upon oral administration a relative bioavailability not less than about 50% by comparison with an orally delivered solution containing celecoxib at the same dosage rate.

(D_{90} less than 200 μm recited in present Claim 85)